Please add the following new claims:

Claim 25 (New):

An isolated, purified, or recombinant signal peptide:

a) consisting of residues –16 to –1, inclusive, of SEQ ID NO: 831, or a fragment thereof; and

b) directing the extracellular secretion of a polypeptide to which said signal peptide is operably linked.

Claim 26 (New):

An isolated, purified, or recombinant signal peptide consisting of an amino acid sequence that has at least 95% identity to the signal peptide of claim 25 and directs the extracellular secretion of a polypeptide to which said signal peptide is operably linked.

Claim 27 (New):

The signal peptide of claim 26, wherein said signal peptide consists of residues –16 to –1, inclusive, of SEQ ID NO: 831.

Claim 28 (New):

A purified polypeptide comprising the signal peptide of claim 25 fused in frame to a heterologous polypeptide.

Claim 29 (New):

A purified polypeptide comprising the signal peptide of claim 26 fused in frame to a heterologous polypeptide.

Claim 30 (New):

The polypeptide of claim 28, wherein said signal peptide consists of amino acids –16 to –1, inclusive, of SEQ ID NO: 831.

Claim 31 (New):

A method of producing the polypeptide of claim 25, comprising the steps of:

a) culturing a host cell capable of expressing said polypeptide under conditions suitable for producing said polypeptide; and

b) isolating and purifying said polypeptide produced by said host cell.

Claim 32 (New):

A method of producing the polypeptide of claim 26, comprising the steps of:

a) culturing a host cell capable of expressing said polypeptide under conditions suitable for producing said polypeptide; and

b) isolating and purifying said polypeptide produced by said host cell.

B1
Cont

Claim 33 (New):

A method of producing the polypeptide of claim 28, comprising the steps of:

a) culturing a host cell capable of expressing said polypeptide under conditions suitable for producing said polypeptide; and

b) isolating and purifying said polypeptide produced by said host cell.

Claim 34 (New):

A method of producing the polypeptide of claim 29, comprising the steps of:

a) culturing a host cell capable of expressing said polypeptide under conditions suitable for producing said polypeptide; and

b) isolating and purifying said polypeptide produced by said host cell.

Remarks

Claims 1, 4-8, 10-13, 17, and 19-24 were pending in the subject application. Applicants acknowledge that claims 1, 4-8, 10-13, 17, 19-21, and 24 have been withdrawn from further consideration as being drawn to a non-elected invention. By this Amendment, claims 22-24 have been canceled and new claims 25-34 have been added. The undersigned avers that no new matter is introduced by this amendment and support for this amendment can be found, for example, at page 3, lines 17-29; page 11; page 12, lines 27-28; page 20, line 34 through page 21, line 6; page 512 of the Sequence Listing; page 96, lines 16-21; and Examples 48 and 49. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 25-34 are currently before the Examiner for his consideration. Favorable consideration of the pending claims is respectfully requested.

Applicants also respectfully request that any requirement to cancel claims not currently under examination be held in abeyance in order to allow for the rejoinder of claims directed to methods of making and/or using the signal peptides claimed herein in light of Patent Office policy related to the treatment of product and process claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b). Applicants acknowledge that the Patent Office may, where appropriate, require applicant, under 35 U.S.C. § 121, to elect claims to either the product or process and that claims directed to the non-elected invention are withdrawn from further consideration under 37 C.F.R. § 1.142. However, the policy indicates that if applicant elects claims directed to the product, and the product is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product will be rejoined. Accordingly, applicants have submitted claims 31-34 to facilitate such a rejoinder and respectfully request that the Patent Office acknowledge that these claims will be rejoined at such time as the product claims (claims 25, 26, 28, and 29 are found allowable.

As an initial matter, on the Office Action Summary page, the Examiner has indicated that the proposed drawing correction filed November 4, 2002 is approved and that corrected drawings are required in reply to the Office Action. Applicants have submitted formal Figures 1-5 with this Amendment. Entry and review of the formal drawings is respectfully requested.

In the Office Action dated November 18, 2002, the Examiner maintains the rejection of claims 22 and 23 under 35 U.S.C. §101. Cancelled claims 22 and 23 were directed to polypeptides comprising the signal peptide of SEQ ID NO: 831. The Examiner asserts that the mere fact that a polypeptide comprises a signal peptide does not automatically provide the invention with a specific and substantial utility and that it takes further research to determine what real world utility the claimed polypeptide possesses. The Examiner further rejects claims 22 and 23 under U.S.C. §112, first paragraph, asserting that, since the claimed polypeptides are not supported by a specific utility, one skilled in the art would not know how to use the claimed polypeptides.

Without prejudice for future prosecution, Applicants have cancelled claims 22 and 23 and added new claims 25 to 30. New claims 25-27 are direct to *signal peptides* consisting of the signal peptide of SEQ ID NO: 831, fragments thereof, or signal peptides that are at least 95% identical to the signal peptide of SEQ ID NO: 831. Furthermore, the claim recites that these signal peptides are capable of directing the extracellular secretion of a polypeptide.

Applicants submit that the signal peptides of claims 25-27 have a specific utility since they direct the extracellular secretion of a polypeptide when fused to a heterologous polypeptide. This function is not a general function that is applicable to any polypeptide. Moreover, Table V (at page 62 of the specification as filed) teaches that SEQ ID NO: 43, which encodes the claimed signal peptide, is expressed in liver, the signal peptides of claims 25-27 are of particular interest for directing protein secretion in liver cells. Applicants also submit that there is no need for further research to characterize the signal peptides of the claims as the sequence and function of these signal peptides is clearly indicated the specification and the sequence listing (see, *e.g.*, page 3, lines 17-29 of the specification, and page 512 of the sequence listing). Accordingly, the function of the signal peptides of claims 25-27 for directing extracellular secretion is disclosed as to a currently available, substantial and credible utility. Additionally, it is respectfully submitted that the use of signal peptides for directing extracellular secretion of polypeptides of interest is well-known to those skilled in the art.

New claims 28-30 are directed to fusion polypeptides wherein the signal peptide of claims 25-27 is fused in frame to a heterologous polypeptide. The attachment of the signal peptides of claims 25-27, in frame, to polypeptides for which secretion is desired is useful, for example, in

directing extracellular secretion of a cytoplasmic polypeptide or for simplifying protein purification. The utility of such heterologous polypeptides for allowing secretion of said polypeptide is illustrated by many prior art references (two such articles are attached hereto). Pecceu *et al.* (*Gene*, 1991; 97:253-8) shows that fusion of mature IL-1 beta to a heterologous signal peptide allowed IL-1 beta to be secreted by the exocytotic pathway. Uchibayashi *et al.* (*J Immunol*, 1989; 142:3901-8) describes the secretory production of the extracellular domain of Fc epsilon receptor II using the signal peptide of IL-6. In view of the above, the signal peptides and fusion polypeptides of new claims 25-30 clearly satisfy the utility requirement under 35 U.S.C. §101. Applicants request (i) the standing rejection under 35 U.S.C. §101; and (ii) the standing rejection under 35 U.S.C. §112, first paragraph, based on the rejection under 35 U.S.C. §101, be withdrawn.

The Examiner rejects claim 22 under 35 U.S.C. §103(a) s obvious over Geneseq Accession No. AAV88297, which is disclosed in WO 98/45437, in view of Watson *et al.* The Examiner indicates that (i) AAV88297 teaches a cDNA sequence encoding a polypeptide comprising amino acids –16 to –1 of SEQ ID NO: 831; and (ii) Watson *et al.* provides the procedure of producing the polypeptide encoded by a cDNA. Thus, the Examiner concludes that there would have been a reasonable expectation of success for one skilled in the art to make the claimed invention at the time the invention was filed.

Applicants first draw the Examiner's attention on the fact that the claimed signal peptide was disclosed in U.S. Patent Application Serial No. 09/057,719, filed April 9, 1998, of which the present application is a continuation-in-part. SEQ ID NO: 831 of the present application corresponds to SEQ ID NO: 1206 of the '719 application (see page 120 of the Sequence Listing). Accordingly, the effective filing date of claims 25-30 is April 9, 1998. WO 98/45437 is an international application published on October 15, 1998. Thus, WO 98/45437 was published later than the effective filing date of claims 25-30 and is not available as prior art. Accordingly, Applicants respectfully request the withdrawal of the standing rejection under 35 U.S.C. §103(a) based on WO 98/45437.

In view of the foregoing remarks and new claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

Frank C. Eisenschenk, Ph.D.
Patent Attorney
Registration No. 45,332
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: 2421 N.W. 41st Street, Suite A-1
Gainesville, FL 32606-6669

FCE/sl
Attachment: Formal Figures 1-5